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EXAMINER

KRASS, FREDERICK F

ART UNIT

PAPER NUMBER

1614

DATE MAILED: 07/31/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/889,530

Applicant(s)

SKIBO, EDWARD B.

Examiner

Frederick Krass

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Specification Informalities

1) The specification contains drawing figures at pages 8, 9, 10 and 11. These should be deleted from the specification and re-submitted as free-standing formal drawings, and the specification amended to contain a "Brief Description of the Drawings" heading.

2) "Scheme 2" at page 5 contains several lines in which the text is illegible.

Claim Informalities

The claims contain a number of informalities which, while not indefinite *per se*, nevertheless render the claims in poor form.

The following corrections are suggested:

- 1) Claim 1, first line, immediately before "neoplastic" there should be inserted ---
a ---
- 2) Claim 2, first line, "yujungamycins" should be singularized, and "have" changed to --- has ---
- 3) Claim 2, last line, immediately after the comma there should be inserted --- or -
- 4) Claim 3, "yujungamycins" should be singularized.
- 5) Claim 6, second line, "has" should be changed to --- have ---

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6) Claim 7, first and second lines, "yujungamycin" should be pluralized and "is" changed to --- are ---

7) Claim 9, second line, "has" should be changed to --- have ---

8) Claim 10, first and second lines, "yujungamyin" should be pluralized and "is" change to --- are ---

Written Description Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim recites the broad term "yujungamycin". The term is clearly meant to be generic in nature, but no written description (other than use of the same broad term) is provided in the specification of the particular class of compounds encompassed by that term. At first blush, one would think a "yujungamycin" was any compound containing the azamitosene core structure shown at page 2, line 11 of the instant specification.

Reading further, however, this becomes unclear; for instance, Table I at page 7 lists only the azamitosene in which the "Z" substituent is -NHCOCH_3 as a "yujungamycin"

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(i.e. yujungamycin A). Thus, the specification provides no written description of specific yujungamycins beyond those having the structure originally recited in claims 5 and 8, as exemplified by the particular species yujungamycin A.

Indefiniteness Rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1) The scope of the term "yujungamycin" is unclear since the specification does not specify whether the term circumscribes those compounds having the azamitosene core structure, regardless of substitution (as the term "steroid" defines that class of compounds having a cyclopentanohydrophenanthrene ring system), or if a particular substitution is required, i.e. amino, acetamido or carbamido as recited in claims 2, 5 and 8. For the same reasons, it is additionally unclear when derivatives of "yujungamycins" would be within the scope of claim 1, and when they would not.

2) Claims 9 and 10, first line of each claim, there is no antecedent basis for a "pharmaceutical preparation", which apparently should be replaced with --- method ---.

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Anticipation Rejection

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1) Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Skibo et al (USP 5,246,955).

Interpreted as broadly as is reasonable, the term "yujungamycin" would encompass those compounds having the azamitosene core structure, regardless of substitution. See the "Written Description" and "Indefiniteness" sections supra. Accordingly, the pharmaceutical preparations of the prior art, which contain tumor-inhibiting amounts of azamitosenes in pharmaceutically acceptable carriers (col. 22, lines 44-53 and col. 24, line 49 et seq.), are viewed as anticipating the subject matter of instant claim 1.

2) Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Skibo et al ("Studies of Pyrrolo[1,2-a]benzimidazolequinone DT-Diapharose Substrate Activity...", *J. Med. Chem.* vol. 40, pp. 1327-1339 (1997)).

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The prior art discloses yujungamycin A and its S(-) enantiomer, a.k.a. 3-carbamido-6-aziridiny-2,3-dihydro-7-methyl-1H-pyrrolo[1,2- α] benzimidazole-5,8-dione (p. 1327, Chart 1, compound 3), which is recovered after synthesis in methanol (p. 1329, second line in the scheme at the top of the page). The compound exhibits *in vitro* activity against melanoma and ovarian cancer (p. 1330, Table 2).

Because methanol is a "pharmaceutically acceptable carrier", the prior art compositions are seen to be fairly anticipated the instantly claimed "pharmaceutical preparations". The same reasoning can also be applied to the buffer solutions used to conduct enzymatic studies on the prior art compounds (see page 1333, the last full paragraph on the page), as well as the media used for *in vitro* antitumor testing.

Obviousness Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skibo et al ("Studies of Pyrrolo[1,2- α]benzimidazolequinone DT-Diapharose Substrate Activity...", *J. Med. Chem.* vol. 40, pp. 1327-1339 (1997)).

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The prior art has been discussed in subsection "2)" of the "Anticipation" section supra, and differs from the instant claims insofar as it does not specifically disclose treating a "host afflicted with a neoplastic disease" such as ovarian cancer. It does, however, clearly test the efficacy of yujungamycin A on ovarian cancer cell lines *in vitro* (Table 2 at page 1330). It would have been obvious in a self-evident manner, therefore, to have used yujungamycin A to treat ovarian cancer in mammals and humans, motivated by the clear indicia of therapeutic efficacy provided by the secondary reference studies, which use *in vitro* testing models recognized in the art as being reasonably predictive of and correlatable to *in vivo* success.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frederick Krass whose telephone number is (703) 308-4335. The examiner can normally be reached on Monday, Tuesday and Thursday from 9am to 5pm, and on Friday from 11am to 7pm. The examiner is off Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0193.

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Frederick Krass
Primary Examiner
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A handwritten signature in black ink, appearing to read 'Frederick Krass', written in a cursive style.